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ANNUAL RESEARCH PROGRESS REPORT

FY 1996

Grand Forks Human Nutrition Research Center

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HUMAN NUTRITION
RESEARCH CENTER
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ANNUAL RESEARCH PROGRESS REPORT

(FY 1996)

GRAND FORKS HUMAN NUTRITION RESEARCH CENTER

**UNITED STATES DEPARTMENT OF AGRICULTURE
AGRICULTURAL RESEARCH SERVICE
NORTHERN PLAINS AREA**

GRAND FORKS, NORTH DAKOTA 58202

MINERAL NUTRIENT REQUIREMENTS
MANAGEMENT UNIT



ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0149753 Year: 96 Project Number: 5450-51000-012-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 50% 5.1.3.4 50%

Title: EFFECTS OF COPPER DEPLETION ON CARDIOVASCULAR
FUNCTION AND METABOLISM

Period Covered From: 03/96 To: 12/96

Progress Report

When rats were fed a diet with a concentration of copper slightly exceeding the average of human diets in the U.S., extra dietary iron produced increased cholesterol in blood, decreased copper in the heart and caused unhealthy enlargement of the heart. When the concentration of dietary copper was increased to slightly exceed that of 84% of U.S. diets, the increase in cholesterol and heart enlargement were unaffected by extra iron, but copper in heart still was decreased. When copper deficiency impairs liver physiology, some of the impairment results from increased iron in liver; the increase in iron in liver cell nuclei substantially exceeds the decrease in copper. Much of the damage of deficiency including heart enlargement results from impaired oxidative defense mechanisms; deficient rats attempt to compensate for decreased defense based on copper by increased defense based on manganese. This compensation is only partially successful as liver damage in deficiency can be seen with electron microscopy. These data are useful to committees who establish recommended dietary allowances and to people who plan human diets and plan research.

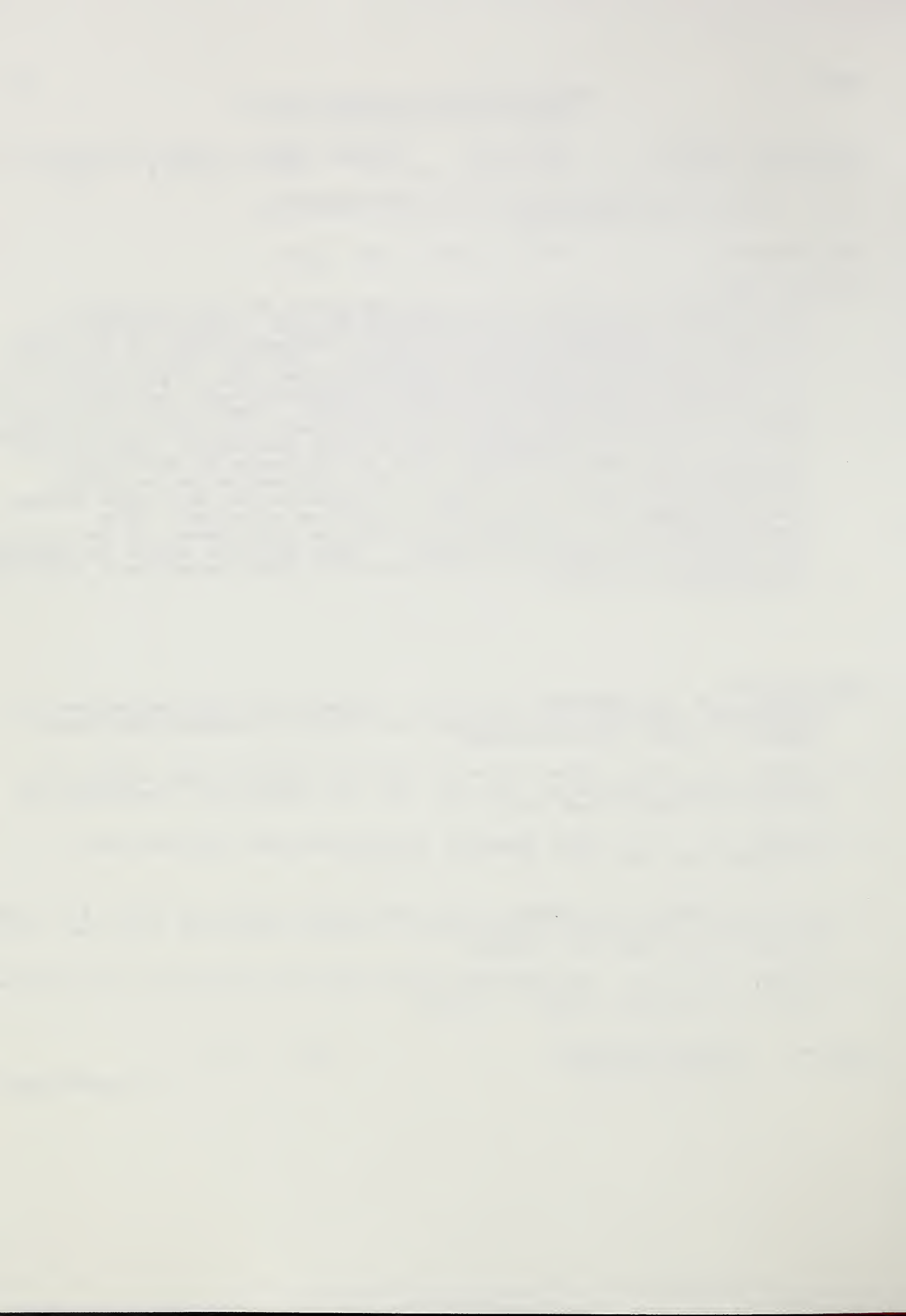
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04. LAI, C-C, HUANG, W-H, KLEVAY, L.M., Gunning III, W.T. and Chiu, T.H. 1996. Antioxidant enzyme gene transcription in copper-deficient rat liver. Free Radical. Biol. Med. 21: 233-240.
05. KLEVAY, L.M. 1996. Iron overload induces hypercholesterolemia when dietary copper is marginal. FASEB J. 10:A294.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0149753 Year: 96 Project Number: 5450-51000-012-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 50% 5.1.3.4 50%

Title: EFFECTS OF COPPER DEPLETION ON CARDIOVASCULAR
FUNCTION AND METABOLISM

Period Covered From: 03/96 To: 12/96

Publications: (Continued)

06. KLEVAY, L.M. 1996. Dietary copper can overcome some adverse effects of iron overload. 9th Intl. Symp. on Trace Elements in Man and Animals, Program and Abstracts, p 75, NRC Press, Ottawa.
07. LYNCH, S.M., MORROW, J.D., KLEVAY, L.M., FREI, B., VITA, J.A. and Keaney, J.F. 1996. Vascular superoxide dismutase deficiency impairs endothelial vasocilator function by two distinct mechanisms. Circulation 94:I-45

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0400377 Year: 96 Project Number: 5450-51000-020-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.2 60% 5.1.3.3 40%

Title: HOMEOSTASIS AND BIOAVAILABILITY OF TRACE ELEMENTS
IN HUMANS AND ANIMALS

Period Covered From: 04/96 To: 12/96

Progress Report

Healthy young women with serum ferritin concentrations in the top, or bottom, 10% of the normal range were fed diets supplying 1 or 10 mg of manganese per day. Manganese status was unaffected by dietary manganese but absorption of manganese in the high ferritin, high manganese group, was one tenth that of the low ferritin, low manganese group. The retention time of manganese in the body was lower in the subjects with greater absorption. Cultured human liver carcinoma cells (Hep-G2) were used to model manganese metabolism in liver. Manganese was actively taken up by Hep-G2 cells; uptake was influenced by calcium and metabolic inhibitors. Once manganese was internalized in the cells, it was quickly excreted by a mechanism involving lysosomes. The bioavailability of selenium in broccoli was studied in rats. Rats were made deficient in selenium by feeding a low selenium diet; selenium status was restored by feeding diets adequate in selenium. Selenium from broccoli did not restore selenium status as fast as other forms of selenium such as selenium salts or selenomethionine, but this was the result of selenium in broccoli being metabolized differently than the other forms of selenium. Freeze-thaw cycles and pH were found to affect direct-reacting copper measurement. These findings are of value in determining the RDA of copper and manganese in humans and in assessing the bioavailability of selenium from foods.

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Accession: 0400377 Year: 96 Project Number: 5450-51000-020-00 D
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Title: HOMEOSTASIS AND BIOAVAILABILITY OF TRACE ELEMENTS
IN HUMANS AND ANIMALS

Period Covered From: 04/96 To: 12/96

Publications: (Continued)

06. FINLEY, J.W., BRISKE-ANDERSON, M. and GREGOIRE, B. 1996. Metabolism of manganese by isolated rat hepatocytes and by the hep-G2 cell line. FASEB J. 10:A819.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0400398 Year: 96 Project Number: 5450-51000-021-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.2 60% 5.1.3.3 40%

Title: BIOAVAILABILITY OF TRACE ELEMENTS, ESPECIALLY IRON
FROM FOOD, & ITS INFLUENCE ON NUTRITURE & FUNCTION

Period Covered From: 04/96 To: 12/96

Progress Report

Absorption control mechanisms in premenopausal women were unable to completely adapt to a lacto-ovo-vegetarian diet. Nonheme iron absorption was reduced by about 70% from this diet compared to a control diet. The diet contained phytic acid, which reduces solubility of iron in the intestine. However, the women's intestinal cells produced less ferritin, a protein that reduces iron absorption by binding the iron until the intestinal cell dies and is excreted into feces. Fecal ferritin excretion was reduced by >50% when the women ate the lacto-ovo-vegetarian diet. From balance data, less calcium was absorbed, and less excreted in the urine, without changing calcium balance on the lacto-ovo-vegetarian diet. Apparent absorption of phosphorus was reduced, in part because some of the phosphorus was in the form of phytic acid. The lacto-ovo-vegetarian diet provided substantially more dietary copper, magnesium, and manganese, but only manganese balance was greater ($p < 0.07$). An animal study failed to confirm reduced startle response in rats marginally depleted of iron; previous startle response effects may have resulted from a comparison with luxuriant amounts of dietary iron. Rat serum ferritin was relatively unresponsive to dietary iron; a 70-fold increase in dietary iron resulted in a 36-fold increase in liver nonheme iron, but not even a two-fold increase in serum ferritin. These results will help health professionals provide advice on obtaining mineral nutrients from practical diets.

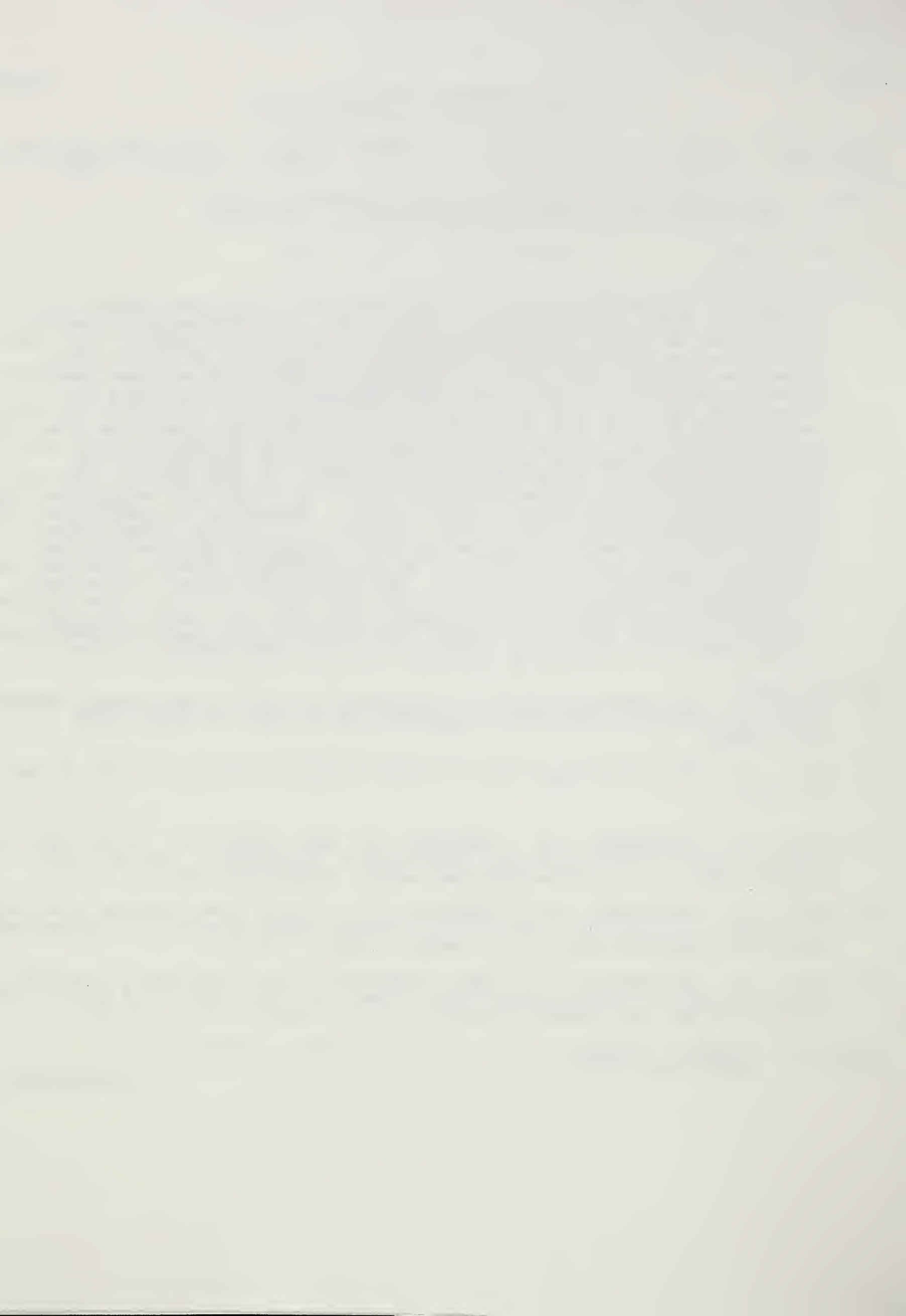
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05. HUNT, J.R. and PENLAND, J.G. 1996. Impaired startle response in growing rats marginally iron-depleted without overt anemia. Ninth Intl Sym on Trace Elements in Man and Animals, Banff, Alberta, Canada, Abstr. p. 45.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0400398 Year: 96 Project Number: 5450-51000-021-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.2 60% 5.1.3.3 40%

Title: BIOAVAILABILITY OF TRACE ELEMENTS, ESPECIALLY IRON
FROM FOOD, & ITS INFLUENCE ON NUTRITURE & FUNCTION

Period Covered From: 04/96 To: 12/96

Publications: (Continued)

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0147555 Year: 96 Project Number: 5450-51000-021-02 S
Mode Code: 5450-10-00 STP Codes: 5.1.3.2 60% 5.1.3.3 40%

Title: IMPROVEMENT OF WHOLE BODY COUNTING EQUIPMENT AND
METHODS FOR MINERAL ELEMENT METABOLIC STUDIES

Period Covered From: 01/96 To: 12/96

Progress Report

The natural incorporation of trace amounts of cadmium from soil has raised concerns about the acceptability of locally grown sunflowers to European markets. Sunflower plants were intrinsically labeled with Cd-115m. Measurement of cadmium retention in the whole body and specific organ sites in three men suggested that absorption of cadmium from sunflower seeds is low (less than 5%), with minimal uptake and storage in the kidney, a critical target organ for cadmium toxicity. An additional detector was added to the human whole body counter this year which increased the capacity for simultaneous detection of isotope retention at specific body sites. An improvement in electronic wiring improved the efficiency of computer calibration of the whole body counter. Plans were also made to improve the computer analysis of the library least squares program to analyze radioactive spectra. Whole body counting measurements were conducted to support human studies investigating the effect of dietary manganese and body iron stores on manganese absorption, the absorption of dietary copper in persons with cardiovascular disease, and the effect of dietary iron bioavailability on biological adaptation in iron absorption. These activities have enhanced the ability to formulate dietary recommendations for the American public.

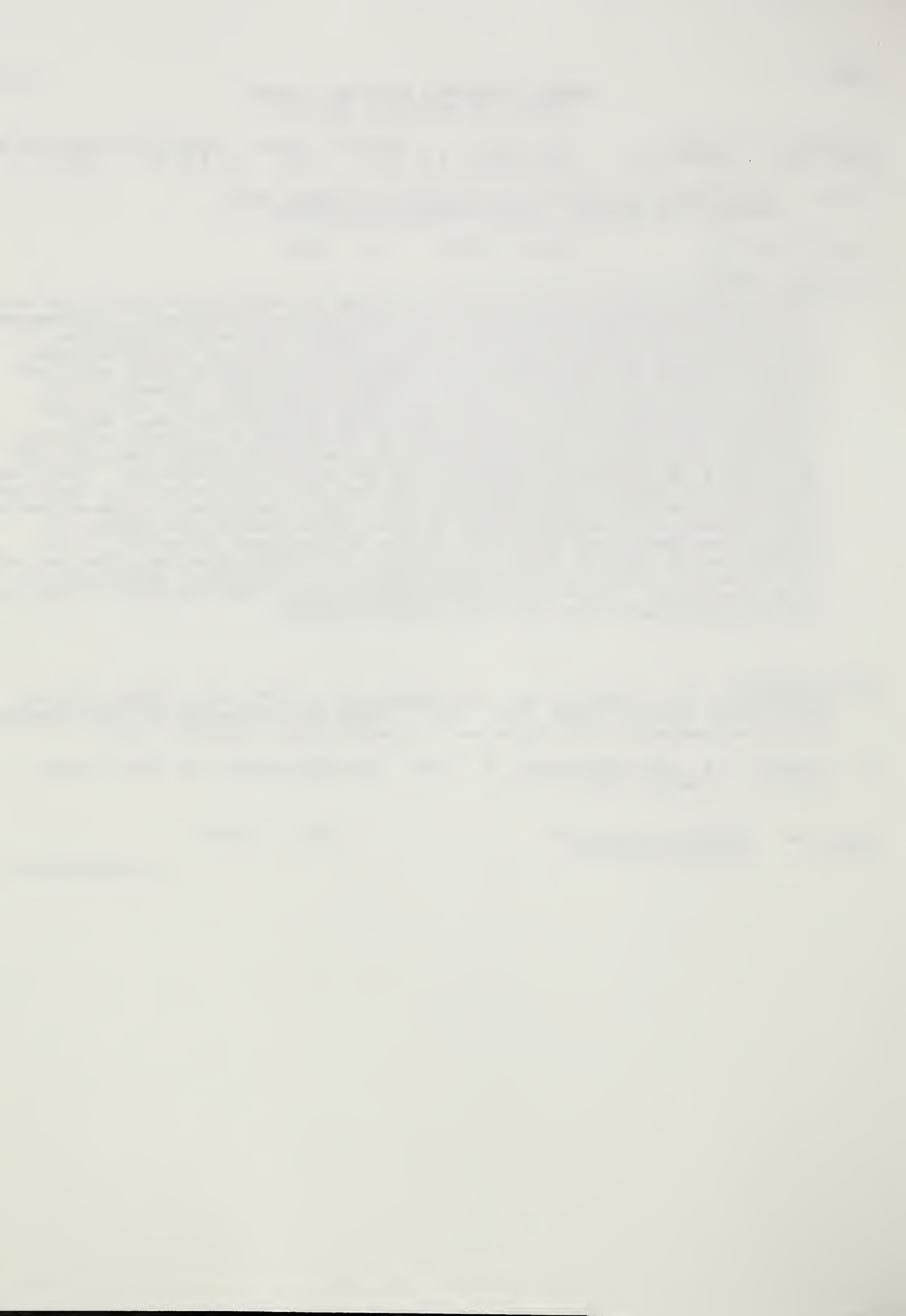
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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0400524 Year: 96 Project Number: 5450-51000-022-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 50% 5.1.3.4 50%

Title: HUMAN MINERAL ELEMENT REQUIREMENTS AND THEIR
MODIFICATION BY STRESSORS

Period Covered From: 05/96 To: 12/96

Progress Report

Experiments have been completed which show that healthy postmenopausal women exhibit changes in indices used to assess the susceptibility to cardiovascular and calcium metabolism disorders simply by reducing the amount of magnesium supplied by a mixed Western diet to about 105 mg/day for 10 weeks. Findings include that of a low magnesium intake increasing abnormal electrical discharges in the heart recorded by a 20-hour holter cardiogram. The dietary restriction of magnesium at a somewhat higher level (150 mg/day for 93 days) also resulted in altered cardiovascular function and energy metabolism in postmenopausal women. Compared to when dietary magnesium was adequate (350 mg/day), a low magnesium intake was associated with a significantly decreased muscle magnesium concentration, increased oxygen uptake and cumulative net oxygen utilization, and increased heart rate during submaximal exercise. Because work output was constant during each exercise test, the increased oxygen consumption and heart rate reflected increased physiological stress to perform the same mechanical work when dietary magnesium was low. These findings will be useful to researchers who seek to identify physiological functions of magnesium and to ascertain whether magnesium is of more nutritional concern than currently acknowledged.

Publications:

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0400524 Year: 96 Project Number: 5450-51000-022-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 50% 5.1.3.4 50%

Title: HUMAN MINERAL ELEMENT REQUIREMENTS AND THEIR
MODIFICATION BY STRESSORS

Period Covered From: 05/96 To: 12/96

Publications: (Continued)

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0400048 Year: 96 Project Number: 5450-51000-022-02 T
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 50% 5.3.1.2 50%

Title: NEW METHODS OF ASSESSMENT OF SPECIFIC SUBOPTIMAL
MINERAL NUTRIENT STATUS IN HUMANS

Period Covered From: 04/96 To: 12/96

Progress Report

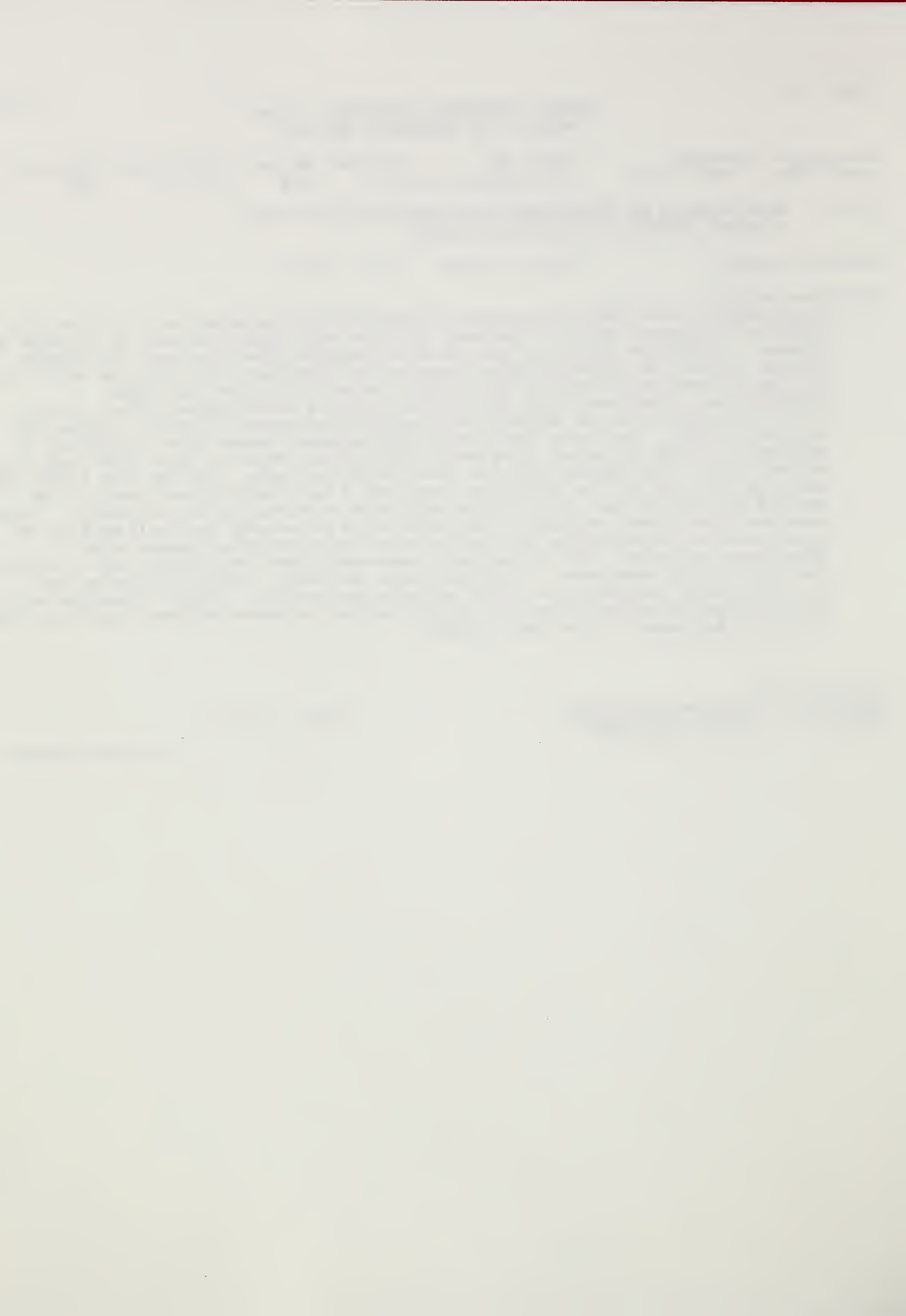
Experiments have been completed investigating the effects of variations in zinc and copper intake of indices of zinc and copper status in animals and humans. Findings from the rat studies suggest that dietary zinc has a direct effect on extracellular superoxide dismutase activity in addition to the antagonistic effect that high dietary zinc has on copper metabolism. Findings from the animal studies also suggest that dietary zinc and copper do not affect beta-amyloid precursor protein expression in the rat brain. Fourteen healthy postmenopausal women just completed a metabolic study in which they were fed a mixed Western diet that supplied either 1 or 3 mg copper/day for two 90-day periods. During the first 90-day period, all of the subjects received 3 mg zinc/day and during the second 90 day period, all of the subjects received 53 mg zinc/day. Blood samples from these subjects are being used to assess the reliability of new potential indicators of zinc status: extracellular superoxide dismutase activity, red blood cell membrane alkaline phosphatase activity, red blood cell membrane 5' nucleotidase activity, metallothioneine and platelet beta-amyloid precursor protein expression. These findings will be of value to scientists for making better recommendations regarding the relative intakes of zinc and copper.

Publications:

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0149894 Year: 96 Project Number: 5450-51530-004-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 25% 5.3.1.2 75%

Title: DEVELOPMENT AND EVALUATION OF METHODS FOR THE
CLINICAL EVALUATION OF MINERAL NUTRITIONAL STATUS

Period Covered From: 05/96 To: 12/96

Progress Report

Twenty-two postmenopausal women completed a study investigating the interaction between dietary copper (Cu) and magnesium (Mg). Serum and ultrafilterable Mg were related to diet Mg; the changes were greater in the subjects who were fed a marginal Cu diet than those supplemented with Cu. A significant interaction between Cu and Mg affected erythrocyte superoxide dismutase activity (ESOD). ESOD was higher in the Cu supplemented subjects than in the marginal Cu subjects when 100 mg Mg/d was fed, but ESOD was not affected by Cu when 300 mg Mg/d was fed. The sequence in which the Mg supplements were given obscured the Mg effects on variables such as serum Mg, % ionized Mg, % ultrafilterable Mg, bound Mg, complexed Mg, cholesterol, glucose, and ESOD; changes were greatest when placebo was fed first and were smaller or lacking when the Mg supplement was fed first. This suggests that prior high Mg inhibits or delays the appearance of Mg deprivation signs. A study with postmenopausal women is in progress to study the effects of dietary zinc (Zn) and Cu on indicators of Cu, Zn, and iron status. Half of the women are being fed a diet containing 1.0 mg Cu/d, the rest are being fed a diet containing 3.0 mg Cu/d. Both groups are receiving 3.0 mg Zn/d for 90 d, followed by 53 mg Zn/d for 90 d. Proposed indicators of Cu and Zn are being evaluated. The preceding is of use to other scientists and to individuals involved in determining the nutritional status of people.

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MINERAL NUTRIENT FUNCTIONS
MANAGEMENT UNIT

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0146625 Year: 96 Project Number: 5450-51000-017-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 100% %

Title: BIOCHEMICAL CONSEQUENCES OF SUBOPTIMAL DIETARY
INTAKE OF TRACE ELEMENTS

Period Covered From: 01/96 To: 12/96

Progress Report

It has been hypothesized that high amounts of dietary zinc will reduce the copper status of animals and humans by inducing metallothionein (MT) which sequesters copper in the intestine. Although adult rats and mice fed high dietary zinc had high intestinal MT, the intestinal copper concentration was low and copper status was not affected. Young rats adapted to high-zinc feeding by reducing intestinal MT but still had low copper status. Mice without a functional MT gene and therefore no inducible MT, still developed low copper status when fed high-zinc diets. Thus, MT is not a major contributor to the poor copper status caused by high zinc intakes. Although cytochrome c oxidase is a copper-dependent enzyme, the relationship between reduced CCO activity and the pathological consequences of copper deficiency are not clear. Culturing HL60 cells in the absence of copper reduced CCO activity and also the activities of mitochondrial respiratory complexes that do not contain copper. Oxidative stress was evident in mitochondria from their elevated protein carbonyl and immunoreactive manganese-dependent superoxide dismutase contents. These findings indicate that reduced CCO activity during copper deprivation promotes oxidative damage that causes a general decline in the function of mitochondrial respiratory complexes.

Publications:

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05. BRISKE-ANDERSON, M., NEWMAN, S.M., and REEVES, P.G. 1996. The effect of in vitro support systems on the morphological characteristics of human colon adenocarcinoma and choriocarcinoma cells. Proc. N.D. Acad. Sci. 50: 48.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0146625 Year: 96 Project Number: 5450-51000-017-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 100% %

Title: BIOCHEMICAL CONSEQUENCES OF SUBOPTIMAL DIETARY
INTAKE OF TRACE ELEMENTS

Period Covered From: 01/96 To: 12/96

Publications: (Continued)

06. REEVES, P.G. 1995. Macro and Ultratrace Mineral Elements. IN: Nutrient Requirements of Laboratory Animals. 4th Edition. National Academy of Sciences.
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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0147990 Year: 96 Project Number: 5450-51000-017-03 T
Mode Code: 5450-20-00 STP Codes: 5.1.3.2 70% 5.2.2.2 30%

Title: HEALTH EFFECTS AND BIOAVAILABILITY OF CADMIUM FROM
SUNFLOWER SEED KERNELS:A HUMAN STUDY

Period Covered From: 01/96 To: 12/96

Progress Report

One of the primary objects of this project is to determine the biological availability of cadmium from sunflower kernels grown in North Dakota and Minnesota. This knowledge will help set standards for allowable limits of this element in food commodities of this type. Thus far, 19 volunteers, 15 women and 4 men have completed the study. Recruitment is underway to identify the remaining 11 men needed to complete the study. A procedure has been developed for measuring isotope enrichments of cadmium in fecal samples by using isotope dilution inductively coupled plasma mass spectroscopy. A liquid-liquid extraction procedure is being tested for the separation of cadmium from other interfering metals. In a 5 M sodium hydroxide fecal digest, sodium diethyldithiocarbamate extracts approximately 35% of the cadmium into chloroform. Comparison of cadmium isotope ratios between a pure standard and an extracted fecal sample, errors of 1.23% for Cd-110/Cd-111 and 0.93% for Cd-113/Cd-111 were found. This indicates that isotope interferences in the extracted fecal sample are minimal. It is hoped that cadmium recoveries above 35% will be achieved before the analysis of samples obtained from the 19 volunteers begins. This information will be critical for consideration by the Codex Alimentarius Commission's Committee on Food Additives and Contaminants when settling limits on cadmium levels in sunflower kernel imports and for reevaluating human lifetime cadmium body burdens from dietary sources.

Publications:

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0400186 Year: 96 Project Number: 5450-51000-018-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.1.3.4 25%

Title: DIETARY TRACE ELEMENTS AND PHYSIOLOGY OF THE
CARDIOVASCULAR AND RELATED SYSTEMS

Period Covered From: 02/96 To: 12/96

Progress Report

The impaired dilation of blood vessels in the microcirculation of copper (Cu)-deficient rats was ameliorated by treatment with the antioxidant enzyme superoxide dismutase; this indicates that the impairment was caused by an oxidative mechanism. The purported antioxidant dimethylsulfoxide (DMSO), which inhibits defects of dietary Cu deficiency in rats, was found to depress food intake and reduce glycation in Cu-deficient rats; this adds to prior evidence that glycation, the undesirable binding of sugar to proteins, also contributes to defects of Cu deficiency. Studies of reduced blood clotting in Cu-deficient rats revealed that the aggregation of blood platelets to one another was increased, that adhesion of platelets to blood vessel endothelial cells was reduced and that these findings were associated with an increase in platelet fibrinogen and a decrease in platelet von Willebrand factor, respectively. A transgenic mouse model, in which the enzyme catalase is overexpressed in the heart, was found to protect the heart against oxidative stressors, e.g. a simulated heart attack, and will be used to study oxidative mechanisms in dietary Cu deficiency. Blood vessels of hearts of Cu-deficient rats constrict similarly, but dilate more slowly, than do those of Cu-adequate rats; this suggests that endothelium-dependent dilation is reduced in hearts as in other organs of Cu-deficient rats. These findings should be useful for developing dietary recommendations for maintaining cardiovascular health.

Publications:

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03. CHEN, Y., SAARI, J.T. and KANG, Y.J. 1996. Suppression of oxidative toxicity in the catalase overexpressing heart of transgenic mice. *Toxicologist* 30:240.
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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0400186 Year: 96 Project Number: 5450-51000-018-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.1.3.4 25%

Title: DIETARY TRACE ELEMENTS AND PHYSIOLOGY OF THE
CARDIOVASCULAR AND RELATED SYSTEMS

Period Covered From: 02/96 To: 12/96

Publications: (Continued)

06. LOMINADZE, D.G., SAARI, J.T., MILLER, F.N. and SCHUSCHKE, D.A. 1996. In vivo platelet thrombus formation in microvessels of copper deficient rats. Int. J. Microcirc. Clin. Exp. 16(S1):182.

Approved: FORREST H NIELSEN
Title: CENTER DIRECTOR

Date: 01/97

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0400106 Year: 96 Project Number: 5450-51000-019-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 90% 5.1.4.3 10%

Title: MINERAL ELEMENT NUTRITION, NEUROPSYCHOLOGICAL
FUNCTION AND BEHAVIOR

Period Covered From: 03/96 To: 12/96

Progress Report

Copper (Cu) and magnesium (Mg) are two minerals of potential relevance to behavior because of their importance in neurotransmitter metabolism and because previous studies have shown that intakes of both minerals affect brain electrophysiology. Two separate controlled studies were conducted to investigate the effects of low dietary Cu (0.05 vs 6.0 ug/g) and Mg (50 vs 500 u/g) on cognition and emotion in mature rats. Low dietary intake for 10 weeks of either mineral was associated with an increase in locomotor activity. Low Cu intake also resulted in more stereotypic (repetitive) behavior during presentation of an auditory stressor, whereas low Mg resulted in increased stereotypic behavior independent of stressor presence. Low Cu intake was associated with poorer performance on measures of learning, whereas low Mg intake was associated with poorer performance on measures of memory. Neither Cu nor Mg showed strong effects on direct measures of anxiety; however, indirect measures of stressor effects during activity monitoring and memory testing suggest that both minerals may impact emotionality. Findings indicate that both Cu and Mg have functional consequences at the behavioral (and possibly emotional) level, which complement earlier findings of effects of these two minerals on brain physiology.

Publications:

01. PENLAND, J.G. and SPEAKER, K.K. 1996. Dietary copper and magnesium effects on activity, learning, memory and anxiety in rats. Proc. N.D. Acad. Sci. 50:57.

Approved: FORREST H NIELSEN
Title: CENTER DIRECTOR

Date: 01/97

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0149978 Year: 96 Project Number: 5450-51520-011-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.2.2.2 25%

Title: BIOCHEMICAL, PHYSIOLOGICAL, AND NUTRITIONAL ROLES
OF CERTAIN ULTRATRACE ELEMENTS

Period Covered From: 03/96 To: 12/96

Progress Report

Findings were obtained from animal studies which suggest that arsenic has a physiological role that affects the enzyme betaine-homocysteine methyltransferase and thus affects methionine recycling. Studies with rats showed that the physiological role of nickel is associated with the folate coenzymes 5-methyltetrahydrofolate and tetrahydrofolate. Findings from experiments using rats indicate that normal amounts of boron in the diet help regulate bone formation during the growth phase in the presence of other nutritional imbalances. Boron reduced the overabundance of trabecular bone deposited during vitamin D repletion (after vitamin D depletion) and improved the underdevelopment of bone caused by feeding insufficient amounts of magnesium. Findings were obtained that showed the BB rat is a sensitive model to use for the study of vanadium nutrition. In this rat both thyroid and glucose metabolism are affected by vanadium deprivation. The concept that fuzzy logic can be used to derive recommended dietary allowances (RDA) for mineral elements was explored. Preliminary results from using fuzzy logic suggest that the RDA for zinc could be set at 9 mg instead of the current 15 mg. The above findings will be of value to scientists, nutrition specialists, and regulatory agencies.

Publications:

01. UTHUS, E.O. and POELLOT, R.A. 1996. Dietary folate affects the response of rats to nickel deprivation. Biol. Tr. Elemn. Res. 52:23-35.
02. KANG, Y.J. and UTHUS, E.O. 1996. Buthionine sulfoximine decreases plasma estradiol and progesterone concentrations in female rats. Biochem. Pharm. 51:567-570.
03. HUNT, C.D. 1996. Dietary boron deficiency and supplementation. IN: R.R. Watson (ed) Trace Elements in Laboratory Rodents, CRC Press, Boca Raton, FL pp. 229-253.
04. HUNT C.D. 1996. Measurements in boron in rodent diets and tissues. IN: R.R. Watson (ed) Trace Elements in Laboratory Rodents, CRC Press, Boca Raton, FL pp. 255-257.
05. HUNT, C.D. and STOECKER, B.J. 1996. Deliberations and evaluations of the approaches, endpoints and paradigms for boron, chromium and fluoride dietary recommendations. J. Nutr. 126:2441S-2451S.

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Title: CENTER DIRECTOR

Date: 01/97

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0149978 Year: 96 Project Number: 5450-51520-011-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.2.2.2 25%

Title: BIOCHEMICAL, PHYSIOLOGICAL, AND NUTRITIONAL ROLES
OF CERTAIN ULTRATRACE ELEMENTS

Period Covered From: 03/96 To: 12/96

Publications: (Continued)

06. UTHUS, E.O. and SEABORN, C.D. 1996. Deliberations and evaluations of the approaches, endpoints and paradigms for dietary recommendations of the other trace elements. J. Nutr. 126:2452S-2459S.
07. WIRSAM, B. and UTHUS, E.O. 1996. The use of fuzzy logic in nutrition. J. Nutr. 126:2337S-2341S.
08. UTHUS, E.O. 1995. Estimation of safe and adequate daily intake for arsenic. IN: W. Mertz, C.O. Abernathy and S.S. Olin (eds), Risk Assessment of Essential Elements, ILSI Press, Washington, DC, pp. 273-282.
09. UTHUS, E.O. 1996. Nickel-low diet and formulation and tissue nickel measurement. IN: R.R. Watson (ed), Trace Elements in Laboratory Rodents, CRC Press, Boca Raton, FL, pp. 355-364.
10. KEEHR, K.A. and HUNT, C.D. 1996. Dietary boron alleviates growth cartilage abnormalities induced by vitamin D deficiency in chicks. Proc. ND Acad. Sci. 50:47.
11. NIELSEN, F.H. 1996. Manganese nutriture affects changes in bone mineral element composition induced by boron deprivation. FASEB J. 10:A819.
12. SEABORN, C.D. 1996. Dietary silicon affects some collagen synthesizing enzymes in rats. FASEB J. 10:A784.
13. HUNT, C.D. and VANDERPOOL, R.A. 1996. Intrinsically labeled ¹⁰B isotope distribution in plasma, brain, heart, and spleen in male rats. FASEB J. 10:A819.
14. MEACHAM, S.L. and HUNT C.D. 1996. Estimated molybdenum intake of American females. FASEB J. 10:A819.
15. UTHUS, E.O. 1996. Compartmental model of arsenic metabolism in hamsters after oral administration of ⁷³/₇₄As. FASEB J. 10:A820.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0149978 Year: 96 Project Number: 5450-51520-011-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.2.2.2 25%

Title: BIOCHEMICAL, PHYSIOLOGICAL, AND NUTRITIONAL ROLES
OF CERTAIN ULTRATRACE ELEMENTS

Period Covered From: 03/96 To: 12/96

Publications: (Continued)

16. POELLOT, R.A. and UTHUS, E.O. 1996. Dietary histidine loading has no marked effect on the interaction between nickel and folic acid in rats. FASEB J. 10:A783.

17. UTHUS, E.O. 1996. Arsenic essentiality in laboratory animals. Society of Toxicology 35th Annual Meeting Abstracts.

Approved: FORREST H NIELSEN
Title: CENTER DIRECTOR

Date: 01/97

UNOFFICIAL

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0146178 Year: 96 Project Number: 5450-51520-011-02 T
Mode Code: 5450-20-00 STP Codes: 5.1.3.4 100% %

Title: THE NUTRITIONAL ROLE OF BORON IN THE INHIBITION OF
SERINE PROTEASES

Period Covered From: 01/96 To: 12/96

Progress Report

Experiments were conducted to examine the mechanisms through which dietary boron delays the onset and severity of induced arthritis. The B-cell and T-cell populations of immune-function cells present in the spleens of rats fed a boron-low diet (<0.2 mg B/kg) were collected and subsequently stimulated to multiply by adding specific agents to the growth solution. The results showed that adding amounts of boron typically found in tissues enhanced the multiplication of T-cells but not B-cells. Higher amounts of boron reduced the multiplication of both T-cells and B-cells. The results of concurrent studies indicated that normal amounts of boron in the diet enhanced the production of antibodies by B-cells. These findings suggest that normal amounts of boron in the diet improve immunity by affecting events early in the immune response process. The above will be of value to scientists and nutrition specialists.

Publications:

01. BAI, Y. and HUNT, C.D. 1996. Dietary boron (B) increases serum antibody concentrations in rats immunized with heat-killed mycobacterium tuberculosis (MT). FASEB J. 10:A819.
02. BAI, Y. and HUNT, C.D. 1996. Adsorption and distribution of boron in rats following a single oral administration of boron. N.D. Acad. Sci. Proc. 50:53.

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Title: CENTER DIRECTOR

Date: 01/97

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0400356 Year: 96 Project Number: 5450-51530-003-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.3.1.1 25%

Title: MINERAL ELEMENTS, PHYSIOLOGICAL FUNCTION &
PERFORMANCE AND BODY COMPOSITION

Period Covered From: 03/96 To: 12/96

Progress Report

A novel use of bioelectrical impedance analysis (BIA) was developed for the routine determination of skeletal muscle mass (SKMM) in humans. With a standard four-electrode arrangement on a thigh, measurements of electrical resistance and reactance were used to develop a model to estimate SKMM in women undergoing weight loss and participating in a controlled exercise program. Reference determinations of thigh SKMM were made with dual x-ray absorptiometry (DXA). Although body weight decreased by 22 kg and physical volume of the thigh decreased by 15%, there was no significant change in thigh SKMM. Also, there was no significant difference between DXA and BIA estimates of thigh SKMM. The effects of copper (Cu) deprivation on mitochondrial structure and function of brown adipose tissue (BAT) were examined. During cold air exposure, Cu-deprived rats had significantly reduced body temperatures. Mitochondrial structure of BAT specimens from Cu-deprived rats was disrupted from a state of orthodox morphology, which stimulates heat production, to a disorientated state in which heat production is impaired. Binding of GDP, a key promoter of the uncoupling of oxidative phosphorylation for heat production, was significantly reduced in BAT in the Cu-deprived rats. These findings will be useful to researchers who seek to determine SKMM, an important body composition variable in humans, and to investigators who study how minerals regulate energy metabolism.

Publications:

01. DROKE, E.A. and LUKASKI, H.C. 1996. Dietary iron and fat affect nonheme iron absorption, iron status and enterocyte aconitase activity and iron concentration in rats. Nutr. Res. 16:977-989.
02. LUKASKI, H.C., BOLONCHUK, W.W., SIDERS, W.A. and MILNE, D.B. 1996. Chromium supplementation and resistance training: effects on body composition, strength and trace...men. Am. J. Clin. Nutr. 63:954-965.
03. LUKASKI, H.C., SIDERS, W.A., HOVERSON, B.S. and GALLAGHER, S.K. 1996. Iron, copper, magnesium and zinc status as predictors of swimming performance. Int. J. Sports. Nutr. 17:535-540.
04. FOSTER, K.R. and LUKASKI, H.C. 1996. Bioelectrical impedance - what does it measure? Am. J. Clin. Nutr. 64:388S-396S.
05. LUKASKI, H.C. 1996. Biological parameters considered in the derivation of the bioelectrical impedance analysis. Am. J. Clin. Nutr. 64:397S-404S.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0400356 Year: 96 Project Number: 5450-51530-003-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.3.1.1 25%

Title: MINERAL ELEMENTS, PHYSIOLOGICAL FUNCTION &
PERFORMANCE AND BODY COMPOSITION

Period Covered From: 03/96 To: 12/96

Publications: (Continued)

06. LUKASKI, H.C. and PENLAND, J.G. 1996. Functional changes appropriate for determining mineral element requirements. J. Nutr. 126:S2354-S2364.
07. LUKASKI, H.C. 1996. Estimation of muscle mass, pp.109-128. IN: A. Roche, S.B. Heymsfield and T.G. Lohman (eds.) Human Body Composition: Methods and Findings. Human Kinetics Publ., Champaign, IL.
08. SMITH, S.M. and LUKASKI, H.C. 1996. Dietary iron: deficiency or excess, pp. 51-58. IN: R.R. Watson (ed.), Methods In Nutrition Research, Vol. 1, Trace Elements in Laboratory Rodents. CRC Press, Boca Raton, FL.
09. LUKASKI, H.C. 1996. Zinc, pp. 157-173. IN: I. Wolinsky and J. Driskell (eds.), Handbook of Sports Nutrition: Vitamins and Minerals. CRC Press, Boca Raton, FL.
10. LUKASKI, H.C. 1995. Human nutrition and the roles beef play in the human diet. Proceedings of the Bovine Connection, Montana and North Dakota Beef Producers, pp 29-32.
11. LUKASKI, H.C., HALL, C.B., MICHELSEN, K.G., and SLEEPER, M.E. 1996. Impaired thermoregulation of copper-deficient rats in the cold is the result of altered thyroid and catecholamine metabolism. FASEB J. 10:A293.
12. DROKE, E.A., JOHNSON, L.K. and LUKASKI, H.C. 1996. Fatty acids affect iron uptake and transport in CACO-2 cells. FASEB J. 10:A249.
13. SIDERS, W.A., LUKASKI, H.C., KRAUSE, D.A., and MATTHYS, L.A. 1996. Predicting daily energy requirements of women. Proc. N.D. Acad. Sci. 50:49, 1996.
14. MICHELSEN, K.G., HALL, C.B., NEWMAN, S.M., DROKE, E.A., SLEEPER, M.E., and LUKASKI, H.C. 1996. Iron deficiency and supplementation impact thermoregulation and brown adipose...cold. Proc. N.D. Acad. Sci. 50:55.
15. TURNER, A.A., BOUFFARD, M. and LUKASKI, H.C. 1996. Measurement error of standard bioelectrical impedance analysis. Abstracts of Tenth International Congress on Circumpolar Health, #426.

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Title: CENTER DIRECTOR

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0400356 Year: 96 Project Number: 5450-51530-003-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.3.1.1 25%

Title: MINERAL ELEMENTS, PHYSIOLOGICAL FUNCTION &
PERFORMANCE AND BODY COMPOSITION

Period Covered From: 03/96 To: 12/96

Publications: (Continued)

16. TURNER, A.A., BOUFFARD, M. and LUKASKI, H.C. 1996. Standard versus modified bioelectrical impedance analysis on reactance measurements. Abstracts of Tenth International Congress on Circumpolar Health, #427.
17. MCLAREN, C.E., KAMBOUR, E.L., MCLACHLAN, G.J., HOUWEN, B., LUKASKI, H.C., MCLAREN, G.D. 1996. Detection of recovery from iron deficiency anemia by patient-specific sequential...of hematological tests. Lab. Hematol. 2:50.
18. LUKASKI, H.C. 1996. Magnesium, zinc and chromium. Abstracts from NIH Workshop on The Role of Dietary Supplements for Physically Active People, pp 73-74.
19. LUKASKI, H.C. 1996. Muscle function and aging: nutritional interventions. Abstracts of the 26th Annual Meeting of American Aging Association and the 11th Annual Meeting of the American College of Clinical Gerontology, p 31.
20. TURNER, A.A., BOUFFARD, M., LUKASKI, H.C. 1996. Generalizability of standard versus modified electrode placement for impedance...measurements. Abstracts of International Symposium on Body Composition Studies, #42.

Approved: FORREST H NIELSEN
Title: CENTER DIRECTOR

Date: 01/97

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INTERIM AND FINAL PROGRESS REPORTS
OF
TERMINATED CRIS WORK UNITS

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0143528 Year: XX Project Number: 5450-51000-009-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.1.3.4 25%

Title: DIETARY TRACE ELEMENTS AND PHYSIOLOGY OF THE
CARDIOVASCULAR AND RELATED SYSTEMS

Period Covered From: 02/91 To: 02/96

Progress Report

Respiration of heart mitochondria, a major site of energy production, was found to be impaired by dietary copper (Cu) deficiency; this impairment was found to be associated with an altered activity of the mitochondrial enzyme, ATP synthase. Reduced dilation of blood vessels was observed in Cu-deficient rats; this finding was related to an interference with nitric oxide-mediated signal transduction by superoxide. Cu deficiency was found to enhance the tissue swelling of inflammation by causing an increase in the number of mast cells from which inflammatory agents such as histamine may be released. Coagulation was shown to be impaired in dietary Cu deficiency; prolonged bleeding time apparently caused by altered attachment of platelets to the vessel wall and a reduced production of von Willebrand factor. A variety of contributions, positive and negative, have been made to the hypothesis that defects occurring in dietary Cu deficiency are caused by oxygen-derived free radicals; this reveals the complexity of the pathology of dietary copper restriction. The view that glycation contributes to defects of dietary Cu deficiency was introduced; findings include the inhibition of defects by an agent that inhibits advanced glycation and alteration of defects by dietary maneuvers that alter glycation. This information should be useful for developing dietary recommendations for maintaining a healthy cardiovascular system.

Publications:

01. SCHUSCHKE, D.A., SAARI, J.T. and MILLER, F.N. 1995. A role for dietary copper in nitric oxide-mediated vasodilation. Microcirculation 2:371-376.
02. SAARI, J.T. 1996. Evidence that dimethyl sulfoxide inhibits defects of dietary copper deficiency by inhibition of glycation. Nutr. Res. 16:467-477.

Approved: J. R. Welsh
Title: AREA DIRECTOR

Date: 06/96

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0144188 Year: XX Project Number: 5450-51000-010-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.2 60% 5.1.3.3 40%

Title: ABSORPTION AND HOMEOSTASIS OF TRACE ELEMENTS

Period Covered From: 04/91 To: 04/96

Progress Report

Human experiments found that copper (Cu) metabolism was affected by sex and age; this suggests that men and women may have different requirements for Cu. Animals were used to develop a new method for measuring readily exchangeable plasma copper (DR Cu), a possible status indicator. Stable isotope methods for Boron (B) were developed to measure uptake and distribution kinetics of B. Boron is quickly and quantitatively absorbed, taken up by the liver, and almost quantitatively excreted in the urine within 3-4 days. Biliary/pancreatic secretions were found to not have a major influence on zinc (Zn) homeostasis. Large changes in Zn intake did not cause a proportionate change in the amount or changes in the chemical form of Zn in these secretions. Men and women were found to absorb and retain manganese (Mn) differently; the difference was related to iron status. Studies with CACO-2 cells, a model of the intestinal epithelium, showed that the Mn moved slowly by diffusion in the direction of absorption, but moved quickly by an active process in the direction of excretion. A human study demonstrated that short-term dietary restriction of selenium (Se) resulted in changes in plasma Se concentration, but no changes in other status indicators. Methods were developed to detect stable isotopes of Se in proteins separated by chromatography or electrophoresis. Stable isotopes and radioactive isotopes of Se labeled the same proteins, which mostly was a medium molecular weight protein.

Publications:

Approved: J. R. Welsh
Title: AREA DIRECTOR

Date: 08/96

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0144337 Year: 96 Project Number: 5450-51000-011-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 50% 5.1.3.4 50%

Title: EFFECTS OF COPPER DEFICIENCY AND ITS MODIFIERS ON
CARDIOVASCULAR METABOLISM AND FUNCTION

Period Covered From: 01/96 To: 03/96

Progress Report

New methods for evaluating electrocardiograms were investigated for application in assessing dietary requirements for copper and magnesium. Variations in heart rate at different times of day appears promising. A complementary study using copper-deficient rats was begun in which a commonly used heart medication will be used to clarify mechanisms of impaired physiology data. The adult daily requirement for magnesium seems to exceed 100 mg when heart muscle irritability is evaluated with electrocardiograms of long duration.

Publications:

Approved: J. R. Welsh
Title: AREA DIRECTOR

Date: 08/96

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0144337 Year: XX Project Number: 5450-51000-011-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 50% 5.1.3.4 50%

Title: EFFECTS OF COPPER DEFICIENCY AND ITS MODIFIERS ON
CARDIOVASCULAR METABOLISM AND FUNCTION

Period Covered From: 03/91 To: 03/96

Progress Report

Because two-thirds of diets in the US contain less copper than the 1.5 mg/day suggested by the National Academy of Science, it is important to identify biochemical and physiological effects that may be impaired when copper intake is insufficient. Mice deficient in copper have both a bleeding tendency and a decreased ability to dissolve blood clots, findings which may relate to similar findings in some people which occur without explanation. Measurement of copper in liver was verified as the best index of copper nutriture; values for other indices can be predicted from liver copper. Copper has been identified as an antioxidant nutrient for cardiovascular health; high blood pressure, high cholesterol and coagulation effects probably all result from impaired defense against oxidative damage. Increased cholesterol from ingestion of zinc supplements is caused by mild copper deficiency and may be accompanied by heart damage. Some of the electrocardiographic abnormalities of copper deficiency result from impaired sodium/potassium function within the electrical system of the heart. Users of this work are most likely to be scientists studying heart disease and basic physiology, the Food and Nutrition Board which sets the recommended dietary allowances, and various committees that comment on nutrition and human health.

Publications:

Publications:

01. Klevay, L.M. 1995. Dietary requirements for metallic elements. Handbook of Metal-Ligand Interactions in Biological Fluids, Vol. 1. Ed: G. Berthon, Marcel Dekker, NY, pp. 287-291.
02. Klevay, L.M. 1995. Copper and cardiovascular disease. Handbook of Metal-Ligand Interactions in Biological Fluids, Vol. 2. Ed: G. Berthon, Marcel Dekker, NY pp. 843-848.

Approved: J. R. Welsh
Title: AREA DIRECTOR

Date: 08/96

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0145351 Year: 96 Project Number: 5450-51000-013-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 80% 5.1.4.3 20%

Title: TRACE ELEMENT NUTRITION, NEUROPSYCHOLOGICAL
FUNCTION AND BEHAVIOR

Period Covered From: 01/96 To: 03/96

Progress Report

Selenium (Se) supplementation (100 ug/d) has been reported to reduce anxiety and depression in both men and women, and we previously found that men fed 28 ug Se/d for 15 weeks reported more while those fed 239 ug Se/d reported less confusion and depression. In the group fed low Se, platelet GSH-Px activity was related to mood states. To determine whether long-term, moderate Se supplementation would have beneficial consequences for mood states in individuals whose usual Se intakes and status were low, we supplemented 33 females and 18 males from Dunedin, New Zealand with 0, 10, 20, 30 or 40 ug Se/d for 6 months and measured mood states monthly. Regression analysis of treatment on time in study (e.g., treatment duration) showed that, among women, 40 ug Se/d increased self-perceived agreeableness, confidence and energy, and decreased total mood disturbance; 30 ug Se/d increased confidence. Se supplementation did not have a statistically significant effect on mood states of men, but the small number of men participating likely resulted in inadequate statistical power. Findings have important scientific and public health implications for those interested in the relationship between nutrition and behavior.

Publications:

01. HUNT, J.R., PENLAND, J.G. and NIELSEN, E.J. 1996. Iron status determined by plasma ferritin in premenopausal women: Associations with laboratory indices, lifestyle, mood, depression...by the MMPI. FASEB J. 9:A975.
02. NIELSEN, F.H. and PENLAND, J.G. 1993. Clinical and biochemical consequences of boron deprivation in humans. Int. J. Toxicol. Occup. Environ. Hlth. 2:34.
03. NIELSEN, F.H. and PENLAND, J.G. 1994. Clinical and biochemical consequences of boron deprivation in humans. IN: Trace and Toxic Elements in Nutrition and Health, Abdulla, M., et al, eds. New Dehli: Jamia Hamdard, pp. 361-374.

Approved: J. R. Welsh
Title: AREA DIRECTOR

Date: 08/96

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0145351 Year: XX Project Number: 5450-51000-013-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 80% 5.1.4.3 20%

Title: TRACE ELEMENT NUTRITION, NEUROPSYCHOLOGICAL
FUNCTION AND BEHAVIOR

Period Covered From: 03/91 To: 03/96

Progress Report

Determined that dietary boron may play a role in normal brain function and behavior of healthy postmenopausal women and older men. Low boron intakes were found to affect brain electrical activity in ways similar to general malnutrition and heavy metal toxicity, and resulted in poorer performance on tasks measuring manual dexterity and short-term memory. Determined that modest increases in dietary calcium may reduce menstrual symptoms, including pain, water retention, and problems with concentration and mood. Calcium may thus play a role in management of menstrual symptoms.

Determined that moderate dietary magnesium deprivation of postmenopausal women increases brain electrical activity consistent with central nervous system and behavioral hyperexcitability previously observed only with more severe deficiencies. Determined in adults that moderate increases in dietary selenium or selenium supplementation improves mood states, reducing depression and confusion, and increasing agreeableness, confidence and energy. Determined that dietary zinc may play a role in cognitive function. Low zinc intakes of adult men resulted in poorer performance on tasks measuring psychomotor skills, attention and memory, while zinc supplementation of school-aged children improved psychomotor, memory and reasoning performance. Developed computer software to automate administration of common neuropsychological tests useful to determining the relationship between nutrition and cognitive and psychomotor function.

Publications:

01. JOHNSON, P.E. and PENLAND J.G. 1996. No effect of Mn or Ca supplementation on menstrual mineral losses in healthy young women. FASEB J. 10:A784.
02. PENLAND, J.G. 1995. Quantitative analysis of EEG effects following experimental marginal magnesium and boron deprivation. Magnesium Res. 8:341-358.
03. PENLAND, J.G., SANDSTEAD, H.H., ALCOCK, N.W., et al. 1996. Cognitive and psychomotor effects of zinc supplementation of urban Chinese children. FASEB J. 10:A290.

Approved: J. R. Welsh
Title: AREA DIRECTOR

Date: 08/96

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0144987 Year: 96 Project Number: 5450-51000-014-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 50% 5.1.3.4 50%

Title: HUMAN MINERAL ELEMENT REQUIREMENTS AND THEIR
MODIFICATION BY STRESSORS

Period Covered From: 01/96 To: 05/96

Progress Report

Some analyses of samples obtained from human volunteers living in a metabolic unit and participating in experiments ascertaining the nutritional importance of magnesium (Mg) were completed. The results indicate that about 160 mg/day may be the Mg requirement for postmenopausal women consuming a diet that does not contain a stressor of Mg metabolism or utilization. One stressor may be dietary carbohydrate because low dietary fructose (less than 5%) compared to high dietary fructose (15% of energy) decreased Mg balance and induced responses indicative of low Mg status (e.g., decreased plasma cholesterol) in postmenopausal women fed about 160 mg Mg/day. Because the increase in fructose was accomplished by reducing complex carbohydrates (starch), the findings suggest that diets high in complex carbohydrates increase the requirement of Mg. In a double-blind crossover experiment in which the variables were about 100 mg and 300 mg Mg/day, the response to Mg deprivation was different when the low Mg diet was fed first than when it was fed last. For example, serum calcitonin was markedly different between the two dietary periods when dietary Mg was high first. When the low Mg diet was fed first, there was very little difference. Just the opposite occurred with serum osteocalcin. The findings indicate that Mg may be of practical nutritional importance for apparently healthy individuals, and are of use to individuals providing nutritional guidance.

Publications:

01. Nielsen, F.H. 1996. Chromium: Charlatan's delight or nutritionists' Concern? In: Perspectives in Nutrition, Third Editions. Eds: G.M. Wardlaw and P.M. Insel, Mosby, St Louis, pp. 556-557.
02. Nielsen, F.H. 1996. Dietary supplementation of physiological amounts of boron increases plasma and urinary boron of perimenopausal women. Proc. North Dakota Acad. Sci. 50:52.
03. Nielsen, F.H. 1996. Chromium. In: Trace Elements in Human Nutrition and Health, World Health Organization, Geneva, pp. 155-160.
04. Nielsen, F.H. 1996. Manganese. In: Trace Elements in Human Nutrition and Health, World Health Organization, Geneva, pp. 163-167.
05. Nielsen, F.H. 1996. Nickel. In: Trace Elements in Human Nutrition and Health, World Health Organization, Geneva, pp. 171-174.

Approved: J. R. Welsh
Title: AREA DIRECTOR

Date: 08/96

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0144987 Year: 96 Project Number: 5450-51000-014-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 50% 5.1.3.4 50%

Title: HUMAN MINERAL ELEMENT REQUIREMENTS AND THEIR
MODIFICATION BY STRESSORS

Period Covered From: 01/96 To: 05/96

Publications: (Continued)

06. Nielsen, F.H. 1996. Boron. In: Trace Elements in Human Nutrition and Health, World Health Organization, Geneva, pp. 175-178.
07. Nielsen, F.H. 1996. Vanadium. In: Trace Elements in Human Nutrition and Health, World Health Organization, Geneva, pp. 180-182.
08. Nielsen, F.H. 1996. Tin. In: Trace Elements in Human Nutrition and Health, World Health Organization, Geneva, pp. 175-178.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0144987 Year: XX Project Number: 5450-51000-014-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 50% 5.1.3.4 50%

Title: HUMAN MINERAL ELEMENT REQUIREMENTS AND THEIR
MODIFICATION BY STRESSORS

Period Covered From: 05/91 To: 05/96

Progress Report

Studies performed on human volunteers demonstrated that the dietary requirements for magnesium, copper, and boron were altered by physiological and nutritional stressors. Dietary magnesium deprivation induced changes in indices used to assess the susceptibility to cardiovascular and calcium metabolism disorders in postmenopausal women; the changes could be modified by copper and boron status. For example magnesium-deficiency induced changes in heart rhythm and plasma cholesterol were enhanced if the women were consuming a diet low or marginal in copper. Low dietary copper and magnesium affected the response to boron deprivation. Some changes caused by boron deprivation, including some of those in calcium metabolism indices such as serum calcitonin and osteocalcin, were seen only when dietary magnesium was low and copper was marginal. The response to copper deprivation was influenced by dietary sulfur amino acids, carbohydrate, and magnesium. For example, copper deprivation depressed erythrocyte copper-zinc superoxide dismutase when dietary fructose was high; replacing fructose with starch resulted in copper deprivation increasing this enzyme. The findings indicate that boron, copper and magnesium are of more practical nutritional importance than acknowledged in the past. The findings should be useful for providing dietary guidance for boron, copper and magnesium.

Publications:

Approved: J. R. Welsh
Title: AREA DIRECTOR

Date: 08/96

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0144249 Year: 96 Project Number: 5450-51000-016-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.2 60% 5.1.3.3 40%

Title: FACTORS INFLUENCING TRACE ELEMENT UTILIZATION AND
REQUIREMENTS IN HUMANS

Period Covered From: 01/96 To: 03/96

Progress Report

Mineral balance of child-bearing age women was determined after 8 weeks of consuming either lacto-ovo-vegetarian or non-vegetarian experimental diets. Compared to the non-vegetarian diet, the vegetarian diet, which contained three times more phytic acid (from whole grains and legumes), resulted in lower apparent absorption and urinary excretion of calcium and phosphorus, and lower fractional apparent absorption of magnesium. These data are in addition to previous isotopic measurements indicating significantly reduced absorption of zinc and of non-heme iron with the vegetarian diet. The vegetarian diet was associated with a 10% reduction in serum cholesterol and cholesterol fractions, without differences in LDL: HDL cholesterol or total: HDL cholesterol ratios. Indices of iron status (hemoglobin, transferrin saturation and ferritin) were unaffected by the vegetarian diet. Plasma ceruloplasmin, copper, and zinc were reduced after consumption of the vegetarian diet. A follow-up study using a copper stable isotope was initiated to investigate copper absorption from these diets.

Publications:

01. Hunt, JR. Position of the American Dietetic Association: Vitamin and mineral supplementation. J Am Dietet Assoc 96:73-77, 1996.

Approved: J. R. Welsh
Title: AREA DIRECTOR

Date: 08/96

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0144249 Year: XX Project Number: 5450-51000-016-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.2 60% 5.1.3.3 40%

Title: FACTORS INFLUENCING TRACE ELEMENT UTILIZATION AND
REQUIREMENTS IN HUMANS

Period Covered From: 04/91 To: 03/96

Progress Report

Determined that typical zinc absorption from US diets is 25-30%. Observed 29% zinc absorption by women and 22% by men from foods designated to represent US diets in the FDA Total Diet Study; 28% and 30% zinc absorption by postmenopausal women from refined diets containing high or low amounts of meat, respectively; and 26% vs 33% zinc absorption, respectively, by premenopausal women from a lacto-ovo-vegetarian diet, and a non-vegetarian diet. Demonstrated that dietary ascorbic acid has minimal influence on iron status of women with chronic low iron stores. Demonstrated that lean meat consumption enhances zinc retention without impairing calcium balance or excessively increasing body iron stores. Zinc from meat was better absorbed than zinc from added mineral supplements. Demonstrated that protein requirements based on nitrogen balance do not increase with aging. Nitrogen balance was similar in postmenopausal women consuming diets with either one or two times the Recommended Dietary Allowance (RDA) for protein; this confirms the RDA for protein in older women. Demonstrated that severe but not marginal iron deficiency reduces serotonin transport into blood platelets. Demonstrated that marginal iron deficiency reduces spontaneous activity in rats. These iron findings suggest that even marginal iron deficiency (as may occur in up to 20% of US women of child-bearing age) may diminish physical activity.

Publications:

Approved: J. R. Welsh
Title: AREA DIRECTOR

Date: 08/96



ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0143832 Year: 96 Project Number: 5450-51520-010-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.2.2.2 25%

Title: BIOCHEMISTRY AND METABOLISM OF CERTAIN ULTRATRACE
ELEMENTS

Period Covered From: 01/96 To: 03/96

Progress Report

The effect of high and low dietary ratios of methionine to cysteine on arsenic deprivation and excess in rats was examined. Preliminary findings suggest that the response to both arsenic deficiency and toxicity is influenced by the dietary methionine to cysteine ratio. A pilot study was performed to establish the parameters to get data for the mathematical modeling of nickel metabolism in rats. It was determined that at least 5 uCi of Ni-63 injected intraperitoneally would be needed and tissues would have to be digested in acid to obtain the radiolabel necessary to determine the distribution of nickel in various organs. Another pilot study determined that methotrexate, a compound that inhibits an important enzyme (dihydrofolate reductase) in folate metabolism (in which nickel may have a role) did not enhance the signs of nickel deprivation in rats. In chicks, physiological amounts of dietary boron and vitamin D had opposite effects on hepatic glycolytic metabolite concentrations. Because the effects of boron on the glycolytic pathway were not modified by vitamin D nutriture, the mechanism through which boron influenced the pathway probably did not involve a direct effect of boron on vitamin D metabolism. Regardless of the mechanism, boron is apparently beneficial because growth of chicks fed marginal vitamin D was improved by boron supplementation. The findings should be of value to scientists, nutrition specialists, and regulatory agencies.

Publications:

Approved: J. R. Welsh
Title: AREA DIRECTOR

Date: 06/96

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0143832 Year: XX Project Number: 5450-51520-010-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.2.2.2 25%

Title: BIOCHEMISTRY AND METABOLISM OF CERTAIN ULTRATRACE
ELEMENTS

Period Covered From: 03/91 To: 03/96

Progress Report

Arsenic deprivation decreases liver S-adenosylmethionine and increases S-adenosylhomocysteine, which can result in DNA hypomethylation that has been correlated with some types of cancer. Physiological amounts of boron modulates energy substrate utilization in an apparent beneficial manner. Boron is closely linked with vitamin D metabolism because boron can ameliorate vitamin D deficiency-induced defects in bone structure. Boron nutriture affects the release of intracellular ionized calcium and the transport of ionized calcium into platelets activated by thrombin; this suggests that boron has a cell membrane function in higher animals. Inadequate copper in the diet of dams slows the development of brain structures involved with learning and memory in their pups. Thus, early copper nutriture may be important for brain development in humans. In rats, germanium as a substitute for silicon, and by itself, affects bone composition, which suggests that germanium may be nutritionally important. Altering methyl metabolism by changing folic acid status affects the response of rats to nickel deprivation, especially in variables related to methionine synthesis from homocysteine, a process dependent upon vitamin B-12 and folate. Thus, nickel may have a physiological role related to folate and/or vitamin B-12 function or metabolism. Silicon deprivation can influence collagen formation in sites other than bone, and thus may be a nutrient of concern in wound healing.

Publications:

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Date: 06/96

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0143968 Year: 96 Project Number: 5450-51530-001-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 25% 5.3.1.2 75%

Title: DEVELOPMENT AND EVALUATION OF METHODS FOR THE
CLINICAL EVALUATION OF MINERAL NUTRITIONAL STATUS

Period Covered From: 01/96 To: 05/96

Progress Report

Eighteen postmenopausal women completed a study that was divided into two 80-day dietary periods. Half were fed a diet containing 1.0 mg copper (Cu)/2000 kcal, the rest were fed a diet containing 3.0 mg Cu/2000 kcal. Both groups received either 100 or 384 mg magnesium (Mg)/2000 kcal in a randomized double blind crossover design to study the effects of dietary magnesium and dietary copper on indicators of copper and magnesium nutritional status. Serum Mg and ionized Mg concentrations were directly related to diet Mg. Serum cholesterol and apolipoprotein B increased and red cell membrane Ca decreased when Mg was added to the diet. The sequence in which the Mg supplements were given obscured the Mg effects on many of the measured variables. This indicated a much stronger carryover effect of Mg than previously believed. The preceding is of use to other scientists and to individuals involved in determining the nutritional status of people.

Publications:

01. Milne, D.B. and Nielsen, F.H. 1996. Effects of a diet low in copper on copper status indicators in postmenopausal women. Am. J. Clin. Nutr. 63:358-64.
02. Milne, D.B. 1996. Adult responses to various short-term dietary copper intakes: Insights on human requirements and indicators of status. Ninth Int. Symp. on Trace Elem. in Man and Animals, TEMA-9, Abstract, p. 74.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0143968 Year: XX Project Number: 5450-51530-001-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 25% 5.3.1.2 75%

Title: DEVELOPMENT AND EVALUATION OF METHODS FOR THE
CLINICAL EVALUATION OF MINERAL NUTRITIONAL STATUS

Period Covered From: 05/91 To: 05/96

Progress Report

A series of metabolic unit studies demonstrated that platelet copper (Cu) and Cu-containing enzymes in blood cells, such as platelet cytochrome c oxidase and erythrocyte superoxide dismutase, are sensitive indicators of Cu status in humans; these indicators are superior to plasma Cu for assessing human Cu nutriture. The blood cell enzymes are sensitive to changes in Cu stores and are not as sensitive as plasma Cu to factors unrelated to Cu nutriture, such as gender, age, and estrogen. Results of these studies also demonstrated that changes in Cu indicators occur when less than 1.25 mg Cu/d is fed and that recovery from mild Cu deprivation may require more aggressive intervention than 2.6 mg Cu/d for periods of up to 35 days. Studies of experimental magnesium (Mg) deprivation in women indicated that although there was a decrease in muscle and erythrocyte Mg concentrations during Mg deprivation, there was a poor correlation between circulating Mg in serum and muscle Mg. Serum ionized Mg was demonstrated to be a potentially sensitive indicator of changes of Mg nutritional status. The order in which Mg supplements or placebos were given affected the apparent response of several indices of Mg status to dietary manipulations. This indicates that the response to short-term Mg depletion and repletion is influenced by the Mg status of the subject upon initiation of treatment. The preceding is of use to other scientists and to individuals involved in determining the nutritional status of people.

Publications:

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Title: AREA DIRECTOR

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0144368 Year: 96 Project Number: 5450-51530-002-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 70% 5.3.1.1 30%

Title: TRACE ELEMENT NUTRITURE, PHYSICAL PERFORMANCE AND
BODY COMPOSITION

Period Covered From: 01/96 To: 03/96

Progress Report

The effects of iron (Fe) nutritional status on mitochondrial structure were examined in male, weanling rats fed Fe-adequate (FeA) or Fe-deficient (FeD) diet and exposed to cold air (4 degrees Centigrade for four hours). Half of the FeD rats were then fed a diet with supplemental Fe (FeS). After an acute cold exposure, interscapular brown adipose tissue (IBAT) was removed and examined by electron microscopy. Mitochondrial structure of the FeD rats was consistent with promoting oxidative phosphorylation for ATP production. In contrast, the mitochondria from FeA and FeS rats exhibited characteristics that indicated a shift toward uncoupling of ATP production and promotion of nonshivering thermogenesis. These structural differences were paralleled by a reduced rate of body temperature decline in the FeA and FeS relative to the FeD rats. These findings provide the first evidence of impaired mitochondrial structural characteristics in the IBAT of FeD animals. This information will be useful to investigators examining the role of mineral elements in energy metabolism.

Publications:

01. LUKASKI, H.C. and SMITH, S.M. 1996. Effects of altered...temp regulation and thermoregulation in the cold. IN: C.M. Blatteis and M.J. Fregley (eds), Am. Physiol. Soc. Hndbk Physiol. Vol 2, NY, NY, Oxford Press pp 1437-1456.
02. MCLAREN, C.E., KAMBOUR, E.L., MCLACHLAN, G.J., LUKASKI, H.C., et al. 1996. Multiple linear regression and finite mixture distribution modelling... IN: University of Queensland Centre for Statistical Research Report #35.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0144368 Year: XX Project Number: 5450-51530-002-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 70% 5.3.1.1 30%

Title: TRACE ELEMENT NUTRITURE, PHYSICAL PERFORMANCE AND
BODY COMPOSITION

Period Covered From: 03/91 To: 03/96

Progress Report

Chromium (Cr) supplementation neither promoted fat loss nor muscle gain in young men participating in strength training. Cr supplementation, however, adversely impacted blood biochemical indices of iron (Fe) nutriture which suggests that Cr supplements may promote Fe deficiency in humans. Obese women provided diets containing copper (Cu) and magnesium (Mg) in amounts found in diets consumed by the US population had significant decreases in whole-body and regional bone mineral status during weight reduction despite participation in a controlled exercise program. Apparently Cu in amounts of 1-1.3 mg/d is inadequate to maintain bone status during weight loss. The role of some mineral elements in the regulation of thyroid hormone status and thermogenesis in animals was shown. Zinc was shown to modulate the production of needed compounds for the synthesis of thyrotropin-releasing hormone in the brain which is under the control of a Zn-containing enzyme, carboxypeptidase H. Cu also was found to regulate the conversion of thyroxine to triiodothyronine via activity of monodeiodinase. Cu-deficient rats had significantly impaired thermoregulation during acute cold exposure that was modulated by decreased induction and expression of certain heat shock proteins and uncoupling protein in the mitochondria of brown adipose tissue. This information will be useful to scientists who seek to define human mineral requirements for health and optimal biological function.

Publications:

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Title: AREA DIRECTOR

Date: 06/96

